Disperse Systems - Emulsions

Hydrophilic-Lipophilic Balance (HLB) System:

Generally, each emulsifying agent has a hydrophilic portion and a lipophilic portion, with one or the other being more or less predominant and influencing in the manner already described the type of emulsion.

A method has been devised whereby emulsifying or surface-active agents may be categorized on the basis of their chemical makeup as to their hydrophilic-lipophilic balance, or HLB.

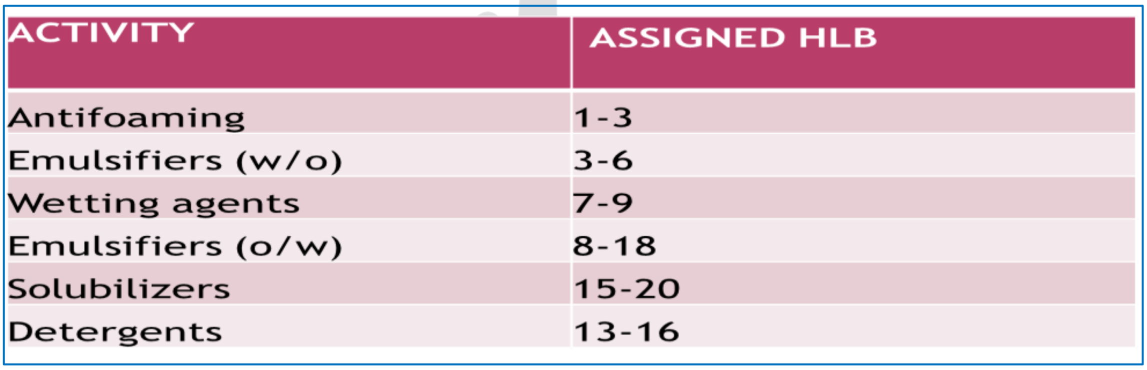
By this method, each agent is assigned an HLB value or number indicating the substance's polarity (the numbers have been assigned up to about 40).

The usual range is between 1 and 20. Each surfactant have an HLB number representing the relative proportions of the lipophilic and hydrophilic parts of the molecule

-Materials that are highly polar or hydrophilic have been assigned higher numbers than materials that are less polar and more lipophilic.

Materials with HLB values of 3 to 6 are highly lipophilic and favor waterin-oil (w/o) emulsions.

- HLB values of about 8 to 18 correspond to emulsifying agents favoring oil-in-water (o/w) emulsions.



ACTIVITY	ASSIGNED HLB
Antifoaming	1-3
Emulsifiers (w/o)	3-6
Wetting agents	7-9
Emulsifiers (o/w)	8-18
Solubilizers	15-20
Detergents	13-16

Required HLB

To ensure emulsion stability, it is necessary to select emulsifying agents having the same or nearly the same HLB value as the oleaginous phase of the intended emulsion.

Certain emulsifying agents of a given HLB value appear to work best with a particular oil phase and this has given rise to the concept required HLB value for any oil or combination of oils.

All oils, waxes and other materials likely to be incorporated into emulsions have an individual "Required HLB."

For example, mineral oil has an assigned HLB value of 4 if a w/o emulsion is desired and a value of 10.5 if an o/w emulsion is to be prepared.

To prepare a stable emulsion, the emulsifying agent should have a required HLB value similar to the one for mineral oil, depending on the type of emulsion desired.

Hydrophilic-lipophilic balance (HLB) method is used for calculating the relative quantities of SAA (emulgents) that necessary for producing a physically stable emulsion.

Blending Emulsifying Agents and Calculations in the HLB System: Stability is achieved by selecting emulsifying agents with HLB values similar to the intended emulsion.

Combining two or more emulsifiers may be necessary to achieve the required HLB value.

HLB values are additive, allowing the blending of surfactants to achieve the desired total HLB value.

The HLB of a mixture of surfactants, for example, a mixture consisting of :

A and B surfactants
Total =1
If fraction A = x
Then fraction B = 1-X
Total HLB= fraction A (x) + fraction B (1 - x)

Calculation the HLB for a mixture of surfactants is assumed to be an algebraic summation of the two HLB numbers

1-Multiply the HLB of each surfactant by its fraction .

2=Add the obtained values to get the total HLB

$$\textbf{Total HLB} = \textbf{HLB}_A\,(X) + \textbf{HLB}_B\,(1-X)$$

- Example: In the Blending two surfactants, what is the ratio of each surfactant? Surfactant A with an HLB value of 8.0, surfactant B with an HLB value of 12.0 to achieve a total HLB value of 9.0.

If fraction A = x

Then fraction B = 1-X

Total HLB = HLB_A (X) + HLB_B (1-X)

9 = 8(X) + 12(1-X)

Fraction A = X= 0.75

Fraction B =1-X = 1- 0.75 =0.25 (3: 1)

-Example:

A formulator is required to formulate an o/w emulsion of the basic formula :

Liquid paraffin	50 g
Emulsifying agents (required HLB 10.5)	5 g
Water to	100 g

Calculate the fraction of Tween 80 (HLB of 15) and Span 80 (HLB of 4.3) used to produce a physically stable liquid paraffin emulsion.

If fraction of tween 80 =X

Then fraction of span 80 =1-X

$HLB_{mixture}$ = HLB_A (X) + HLB_B (1-X)

10.5 =15 * (x) + 4.3 *(1-x)

Example: o/w Emulsion

Liquid petrolatum (Required HLB 10.5) 50 g

Emulsifying agents 5 g

Sorbitan monooleate (HLB 4.3)

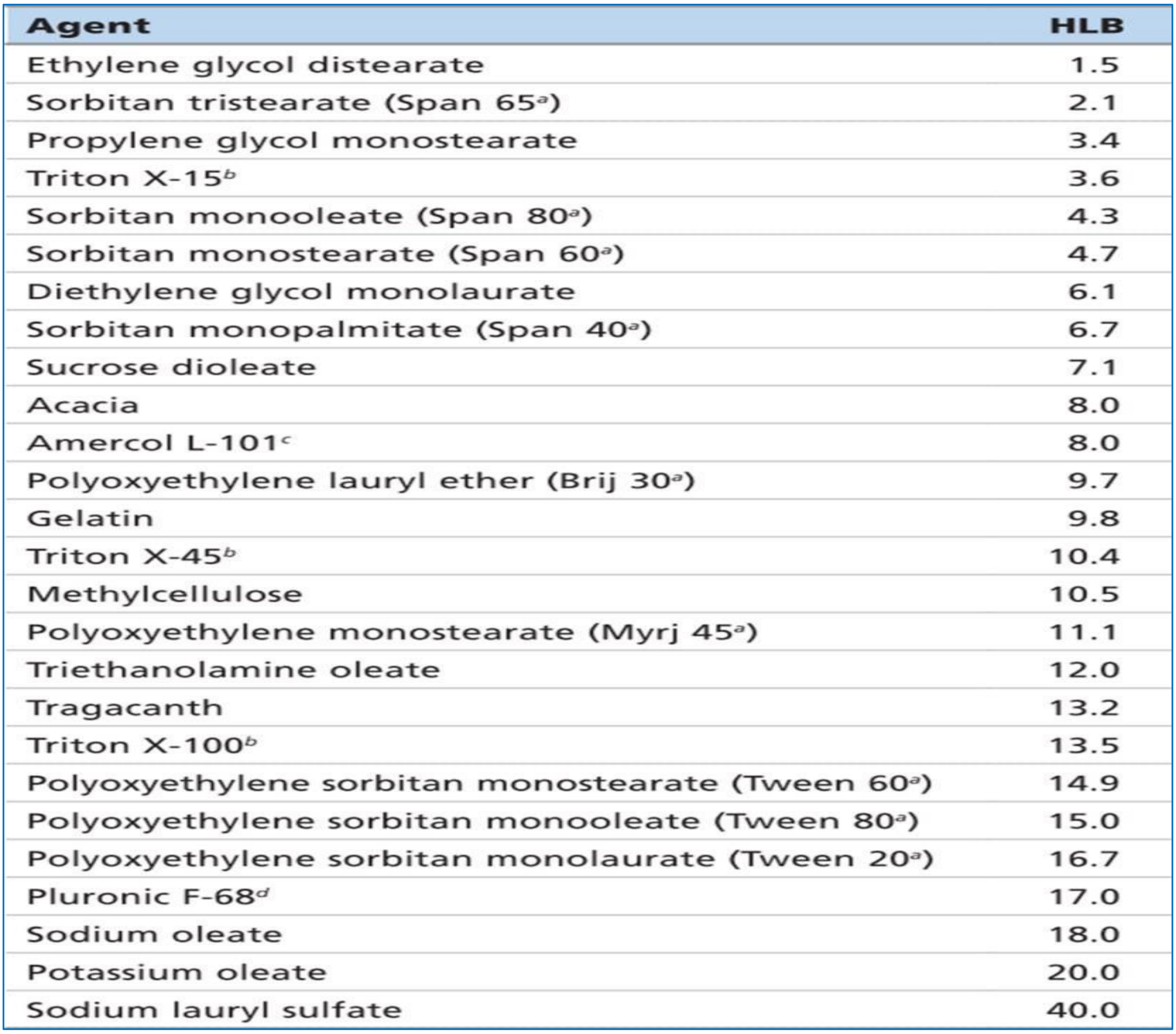
Polyoxyethylene 20 sorbitan monoleate (HLB 15.0)

Water, qs 100 g

By simple algebra, it can be shown that 4.5 parts by weight of sorbitan monooleate blended with 6.2 parts by weight of polyoxyethylene 20 sorbitan monooleate will result in a mixed emulsifying agent having the required HLB of 10.5.

Because the formula calls for 5 g, the required weights are 2.1 and 2.9 g, respectively. The oil-soluble sorbitan monooleate is dissolved in the oil and heated to 75°; the water-soluble polyoxyethylene 20 sorbitan monooleate is added to the aqueous phase that is heated to 70°. At this point, the oil phase is mixed with the aqueous phase and the whole is stirred continuously until cool.

The formulator is not restricted to these two agents to produce a blend with an HLB of 10.5. There are various proportions required, using other pairs of emulsifying agents,



Agent	HLB
Ethylene glycol distearate	1.5
Sorbitan tristearate (Span 65[a])	2.1
Propylene glycol monostearate	3.4
Triton X-15[b]	3.6
Sorbitan monooleate (Span 80[a])	4.3
Sorbitan monostearate (Span 60[a])	4.7
Diethylene glycol monolaurate	6.1
Sorbitan monopalmitate (Span 40[a])	6.7
Sucrose dioleate	7.1
Acacia	8.0
Amercol L-101[c]	8.0
Polyoxyethylene lauryl ether (Brij 30[a])	9.7
Gelatin	9.8
Triton X-45[b]	10.4
Methylcellulose	10.5
Polyoxyethylene monostearate (Myrj 45[a])	11.1
Triethanolamine oleate	12.0
Tragacanth	13.2
Triton X-100[b]	13.5
Polyoxyethylene sorbitan monostearate (Tween 60[a])	14.9
Polyoxyethylene sorbitan monooleate (Tween 80[a])	15.0
Polyoxyethylene sorbitan monolaurate (Tween 20[a])	16.7
Pluronic F-68[d]	17.0
Sodium oleate	18.0
Potassium oleate	20.0
Sodium lauryl sulfate	40.0

Preparation Methods

Various methods are employed for emulsion preparation, ranging from small-scale laboratory techniques to large-scale industrial processes. Each method has its advantages and is chosen based on the nature of components and desired emulsion characteristics

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Small-Scale Emulsion Preparation Methods

-Laboratory Equipment:

Small-scale emulsions can be prepared using equipment like:

1-Dry Wedgwood or porcelain mortar and pestle,

2.Mechanical blenders such as milkshake mixers, hand homogenizers, or 3. Simple prescription bottles.

-Laboratory Techniques:

In the small-scale extemporaneous preparation of emulsions, three methods may be used. They are:

1. The continental or dry gum method
2-The English or wet gum method
3-The bottle or Forbes bottle method

-The continental or dry gum method:

The continental or dry gum method involves triturating the emulsifying agent (e.g., acacia) with oil before adding water (**addition of external phase to the internal phase**).

The continental method is also referred to as the **4:2:1 method** because for every **four parts** by volume of **oil**, **two parts of water** and **one part of gum** are added in preparing the initial or primary emulsion. For instance, if 40 mL of oil is to be emulsified, 20 mL of water and 10 g of gum would be employed in the primary emulsion.

In this method, the acacia or other o/w emulsifier is triturated with the oil in a perfectly dry Wedgwood or porcelain mortar until thoroughly mixed. After the oil and gum have been mixed, the **two parts of water** are added **all at once**, and the mixture is triturated immediately, rapidly, and continuously until the primary emulsion is formed.

A mortar with a rough rather than smooth inner surface must be used to ensure proper grinding action and reduction of the globule size. A glass mortar is too smooth to produce the proper reduction of the internal phase.

The emulsion is transferred to a graduate and made to volume with water previously swirled about in the mortar to remove the last portion of emulsion.

◇ -English or Wet Gum Method:

The English or wet gum method creates a mucilage of the emulsifying agent with water before slowly incorporating oil (**addition of internal phase to the external phase**).

By this method, the same proportions of oil, water, and gum are used as in the continental or dry gum method, but the order of mixing is different. A mucilage of the gum is prepared by triturating in a mortar granular acacia with twice its weight of water.

The oil is then added slowly in portions, and the mixture is triturated to emulsify the oil. After all of the oil has been added, the mixture is thoroughly mixed for several minutes to ensure uniformity. Then, the other formulative materials are added, and the emulsion is transferred to a graduate and brought to volume with water.

◇ -Bottle or Forbes bottle method:

The bottle or Forbes bottle method is suitable for volatile oils or oleaginous substances of low viscosities, involving shaking the mixture in a capped bottle.

Powdered acacia is placed in a dry bottle, two parts of oil are added, and the mixture is thoroughly shaken in the capped container. A volume of water approximately equal to that of the oil is then added in portions and the mixture thoroughly shaken after each addition.

When all of the water has been added, the primary emulsion thus formed may be diluted to the proper volume with water or an aqueous solution of other formulative agents

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Important considerations on emulsion preparation

-Prior to mixing, all the water soluble ingredients are dissolved in the aqueous phase and all the oil-soluble components are dissolved in the oil

-Solid substances such as preservatives, stabilizers, colorants, and any flavoring material are usually dissolved in a suitable volume of water (assuming water is the external phase) and added as a solution to the primary emulsion .

-If fats waxes or SAA that are solids or semisolid at room temperature are needed, warm the two phases, the aqueous phase temperature is raised 2-3C° above that of oil phase, so that no local crystallization of waxes takes place upon mixing of the two phases

-Any substances that might interfere with the stability of the emulsion or the emulsifying agent are added as near last as is practical .

-Alcohol has a precipitating action on gums such as acacia, thus no alcohol or solution containing alcohol should be added directly to the primary emulsion, because the total alcoholic concentration of the mixture would be greater at that point than after other diluents were added.

-When all necessary agents have been added, the emulsion is transferred to a graduate and made to volume with water previously swirled about in the mortar to remove the last portion of emulsion .

-Forbes bottle method is not suited for viscous oils because they cannot be thoroughly agitated in the bottle when mixed with the emulsifying agent .

-When the intended dispersed phase is a mixture of fixed oil and volatile oil, the dry gum method is generally employed

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◇ Auxiliary Methods:

An emulsion prepared by either the wet gum or the dry gum method can generally be increased in quality by passing it through a hand homogenizer.

In this apparatus, the pumping action of the handle forces the emulsion through a very small orifice that reduces the globules of the internal phase to about 5 j.lm and sometimes less.

The hand homogenizer is less efficient in reducing the particle size of very thick emulsions.

In Situ Soap Method (Nascent soap method):

The two types of soaps developed by this method are calcium soaps and soft soaps. Calcium soaps are w/o emulsions that contain certain vegetable oils, such as oleic acid, in combination with limewater (Calcium Hydroxide Solution, USP).

They are prepared simply by mixing equal volumes of the oil and limewater. The emulsifying agent in this instance is the calcium salt of the free fatty acid formed from the combination of the two entities. In the case of olive oil, the free fatty acid is oleic acid, and the resultant emulsifying agent is calcium oleate.

◇ Large-scale preparation

On a larger scale, mixing tanks equipped with high-speed impellers are used for emulsion formation.

- Colloid mills or large homogenizers may be employed to refine the emulsion further.

Industrial homogenizers have the capacity to handle as much as 100,000 L of product per hour.

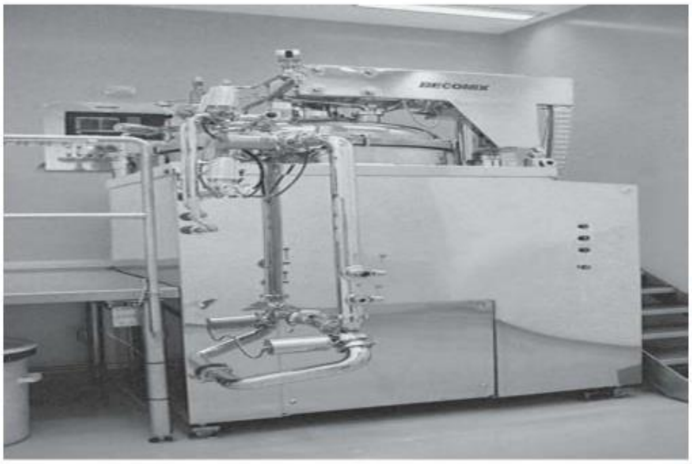


FIGURE 14.5. An industrial mixer for manufacture of disperse systems, including suspensions and emulsions. (Courtesy of Perrigo Company plc.)

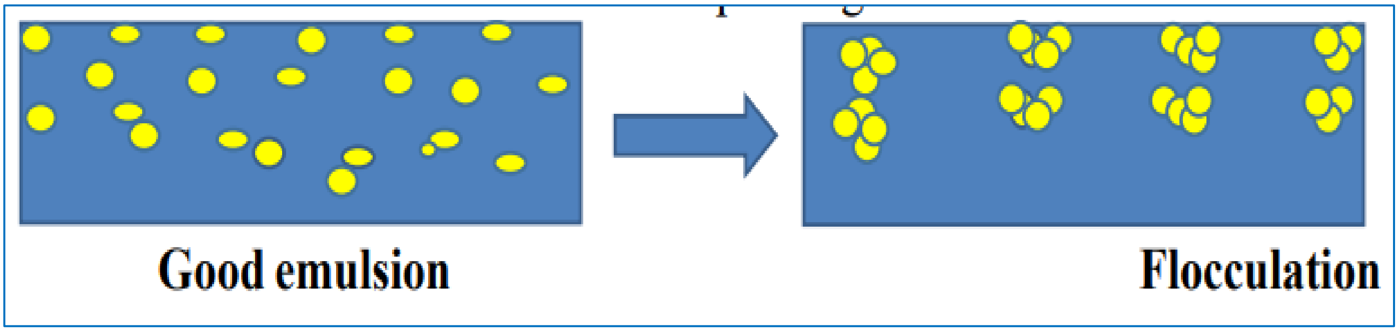
◇ Stability of Emulsions

The instability of emulsions can be categorized as follows:

1- Flocculation
2-Creaming or sedimentation
3-Coalescence or aggregation
4-Cracking or breaking
5-Phase separation

-Flocculation

This process refers to aggregation or joining droplets together (without any change in primary droplet size) to form a large units or clumps (floccules) which rise or settle in the emulsion depending on their densities.



Aggregates of globules of the internal phase have a greater tendency than do individual particles to rise to the top of the emulsion or fall to the bottom. Such a preparation of the globules is termed the creaming of the emulsion, it is a reversible process.

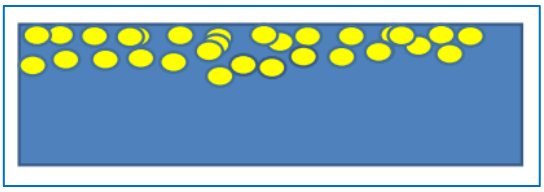
Creamed emulsion can be restored to its original state by gentle agitation, if insufficient shaking is employed before each dose, improper dosage of the internal phase substance may result.

According to the Stokes equation the rate of separation of the dispersed phase of an emulsion may be related to such factors:

1. The particle size of the dispersed phase,
2. The difference in density between the phases,
3. The viscosity of the external phase.

-Larger particle size, greater density difference, and lower viscosity increase the rate of creaming.

Upward creaming takes place in unstable emulsions of the o/w or the w/o type in which the internal phase has a lesser density than the external phase. Downward creaming takes place in unstable emulsions in which the opposite is true



Strategies for enhanced the stability:

1-The globule or particle size should be reduced as fine as is practically possible,

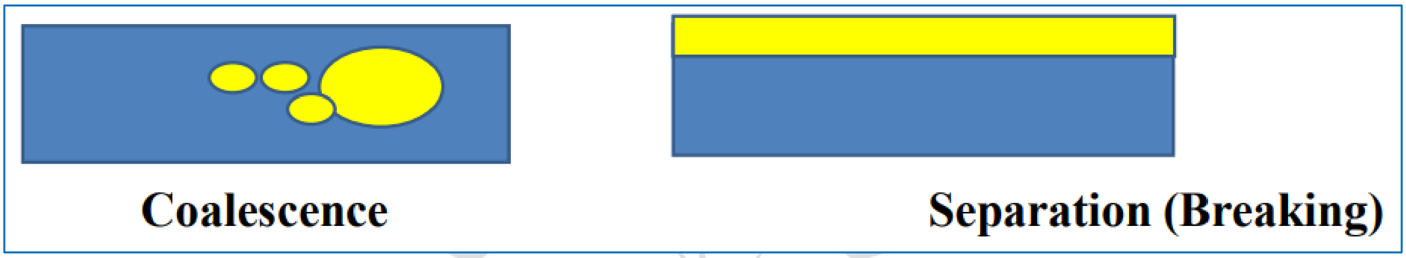
2-The density difference between the internal and external phases should be minimal,

3-The viscosity of the external phase should be reasonably high.

◇ -Coalescence and Breaking (Cracking)

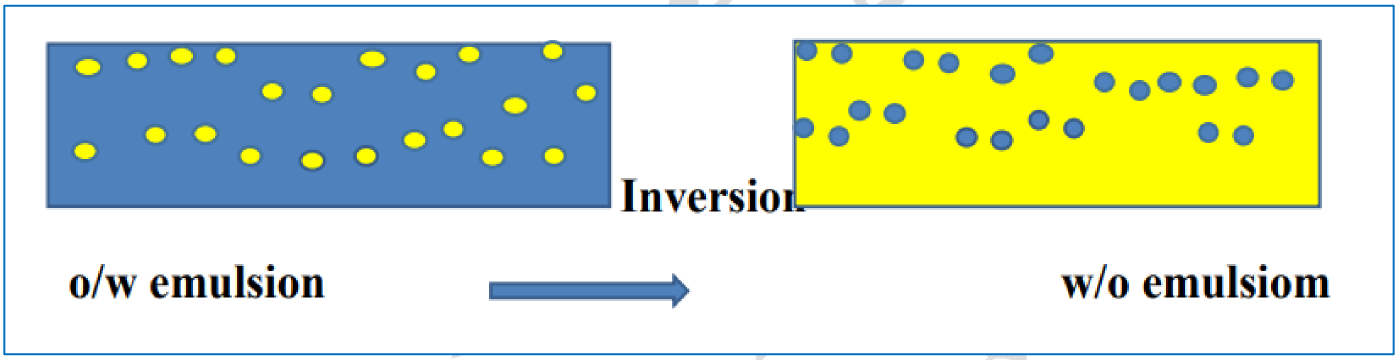
If the droplet contacts another droplet, coalescence will occur to produce a single droplet of greater diameter and, the surface area of the new droplet will be less than the surface areas of the two individual droplets. This process will continue until there is complete phase separation (i.e. two liquid layers occur). Separation of the internal phase from the emulsion is called breaking, and the emulsion is described as being cracked or broken.

This is irreversible, because the protective sheath about the globules of the internal phase no longer exists. If an emulsion has cracked it cannot be recovered or redispersed by shaking.



◇ -Phase Inversion

It is the process of an exchange between the disperse phase and the medium. For example, an o/w emulsion may with time or change of conditions invert to a w/o emulsion (occurs when the dispersed phase exceed a theoretical maximum of 74% of the total volume).



Consideration for temperature, light, environmental factors and storage

-Generally, care must be taken to protect emulsions against extremes of cold and heat. Freezing and thawing coarsen an emulsion and sometimes break it. Excessive heat has the same effect.

-The presence of light, air, and contaminating microorganisms can adversely affect the stability of an emulsion; appropriate formulative and packaging steps are usually taken to minimize such hazards to stability .

-For light-sensitive emulsions, light-resistant containers are used.

-For emulsions susceptible to oxidative decomposition, antioxidants may be included in the formulation and adequate label warning provided to ensure that the container is tightly closed to air after each use.

Preservation of emulsion

Many molds, yeasts, and bacteria can decompose the emulsifying agent, disrupting the system. Because fungi (molds and yeasts) are more likely to contaminate emulsions than are bacteria, fungistatic preservatives, commonly combinations of methylparaben and propylparaben, are generally included in the aqueous phase of an o/w emulsion.

-Alcohol in the amount of 12% to 15% based on the external phase volume is frequently added to oral o/w emulsions for preservation.

Therapeutic examples of Oral and Topical Emulsions

• Oral Emulsions -Mineral Oil Emulsion:

-Mineral oil emulsion, or liquid petrolatum emulsion, is an o/w emulsion prepared from the following materials: Mineral oil, acacia, syrup, vanillin, alcohol, and purified water.

-Preparation by the dry gum method (4:2:1).

-Used as a lubricating cathartic with enhanced palatability compared to plain mineral oil.

-Commercial variations may include additional cathartic agents.

-Castor Oil Emulsion:

-Indications: Laxative for constipation and colon preparation for diagnostic examinations.

-Simethicone Emulsion:

-Indications: Defoaming agent for relief of gastrointestinal gas symptoms.

• Topical Emulsions

-Lotions

Many hand and body lotions for dry skin are o/w emulsions.

A number of topical emulsions, or lotions, are used therapeutically to deliver a drug systemically. An example is Estrasorb, which contains estradiol for menopausal symptom relief.

-Shampoos:

- Shampoos are **solution, emulsion, or suspension** dosage forms used for hair and scalp cleansing.

-Liniments

Liniments are **alcoholic** or **oleaginous solutions** or **emulsions** of various medicinal substances intended to be rubbed on the skin

-The vehicle for a liniment should therefore be selected for the type of action desired (**rubefacient, counterirritant, or massage**) and also on the solubility of the desired components in the various solvents.

-All liniments should bear a label indicating that they are suitable only for external use and must never be taken internally.

-Liniments that are **emulsions** or that contain insoluble matter must be shaken thoroughly before use to ensure even distribution of the dispersed phase, and these preparations should be labeled shake well.

-liniments are prepared in the same manner as **solutions, emulsions, or suspensions**